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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,096	06/15/2000	David J. Diller	1073.060	8927

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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/595,096	DILLER ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 21-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,10,21-27,29 and 30* is/are rejected.

7)☒ Claim(s) *8 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.D

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/27/05 has been entered.

All rejections previously of record are hereby withdrawn in view of the claim amendments filed 4/27/05. Claims 1-10 and 21-30 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 9, 21-27, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over MCMARTIN et al. (J. Comp-Aided Molec. Design (1997) vol. 11, no. 4, pp. 333-344) in view of WANG et al. (Proteins (1999) vol. 36, no. 1, pp. 1-19).

MCMARTIN teaches a computerized method of docking a ligand to a protein to determine ligand conformations likely to bind to the protein wherein he creates pseudo-receptors and determines "hot-spots' or putative binding sites in the receptor (pp. 340-341), then matches solution conformations of ligands to the "hot-spot" and optimizes the position of the ligand by allowing only the ligand atoms to move; i.e. the receptor is held fixed (p. 341). MCMARTIN teaches that ligand conformers may be saved (p. 335), and teaches that a three-dimensional database or library of structures may be used in his method (pp. 337-339). MCMARTIN teaches use of grid-mapping to identify and model a binding site or "hot spot" (p. 337). MCMARTIN also teaches comparison of energies and elimination of positions with scores above a cutoff (i.e. with a steric "clash"), p. 337. MCMARTIN teaches optimizing his hydrogen bond geometries using an algorithm (p. 340), and teaches that his ligand may be held fixed before his optimization step (p. 341), but does not specifically teach calculating a score for an optimized position using a potential function.

WANG teaches a method of docking ligands to a receptor/protein wherein a variety of conformers are selected and docked into a binding site as a rigid

body, then the structure is refined by holding the receptor rigid while simultaneously optimizing bond lengths and angles, and torsional angles of the ligand (pp. 6-7). WANG teaches that the "best" structures are then selected from among the optimized conformers (p. 7), thus his conformers are necessarily ranked. WANG further teaches that at least one scoring function in his method is a potential energy function (p. 3).

It would have been obvious to one of ordinary skill in the art at the time of invention to have included the scoring and ranking of optimized conformers of WANG in the method of MCMARTIN where the motivation would have been to improve prediction of binding structures and reduce the cost and time of the docking protocol, as taught by WANG (p. 16).

Claims 10 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over MCMARTIN et al. (J. Comp-Aided Molec. Design (1997) vol. 11, no. 4, pp. 333-344) in view of WANG et al. (Proteins (1999) vol. 36, no. 1, pp. 1-19) as applied to claims 1-7, 9, 21-27, and 29 above, and further in view of ZHAO (US 5,889,528).

MCMARTIN and WANG make obvious a computerized method of docking a ligand to a protein to determine ligand conformations likely to bind to the protein, wherein the position of the ligand is optimized by holding the protein rigid and allowing translation, orientation and rotatable bonds to vary, as set forth above. MCMARTIN and WANG do not teach optimizing using a Broyden-Fletcher-Goldfarb-Shanno algorithm.

ZHAO teaches that structural analysis using an iterative technique may be improved using a BFGS algorithm (col. 4, lines 35-55).

It would have been obvious to one of ordinary skill in the art at the time of invention to have included the BFGS algorithm of ZHAO in the optimization step of MCMARTIN and WANG where the motivation would have been to improve the iterative step of structure analysis, as taught by ZHAO (col. 4, lines 35-40). One skilled in the art would reasonably have expected success in including the BFGS algorithm of ZHAO in the method of MCMARTIN and WANG because all teach optimizing relationships between structures using iterative calculations.

Allowable Subject Matter

Claims 8 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: the prior art does not teach or fairly suggest use of the algorithm recited in claims 8 and 28.

Conclusion

Claims 1-7, 9-10, 21-27, and 29-30 are rejected; claims 8 and 28 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number

is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
7/11/05